

Amendments to the Specification:

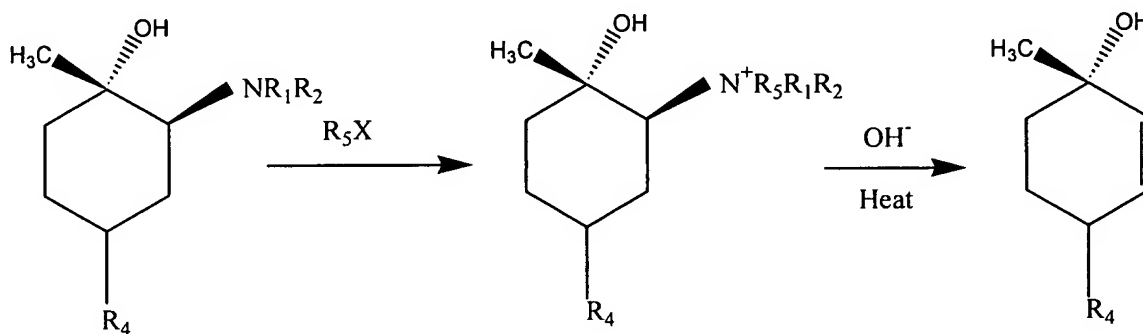
Please amend the specification by adding the following paragraph to page 1 after the title:

--CROSS REFERENCE TO RELATED APPLICATIONS

This application is a national stage application of PCT/US2004/011509, filed April 14, 2004, which claims the benefit of U.S. Provisional Application No. 60/465,046, filed April 24, 2003.---

Please amend the paragraph beginning on page 7, line 13, as follows:

--An alternative embodiment for the conversion of the amine adduct to (+)-p-mentha-2,8-diene-1-ol or an analog thereof is illustrated below:



Formula ~~(2b)~~ (2a)

Formula ~~(6b)~~ (6a)

Formula ~~(5b)~~ (5a)

wherein R₁ and R₂ are H, alkyl or aryl;

wherein R₅ is an H, aryl or alkyl;

wherein R₄ is an alkyl, alkenyl or alcohol; and

wherein X is a halide. --

Please amend the paragraph beginning at page 9, line 14, as follows:

--Upon completion of the reaction, the ethanol was distilled off from the reaction mixture under vacuum to give a light yellow oil. The oil was then re-dissolved into 200 ml of chloroform, and the resulting solution was washed with 100 ml of deionized water twice and 100 ml of brine once, and finally dried with anhydrous MgSO₄. The solid was filtered out and the

Amendment B

Inventor(s) Name: Gu, et.al.

Attorney Docket No.: 1559 WO/US

solvent removed under vacuum to give a light yellow oil. The reaction product was analyzed by HPLC and compared to an authentic sample. The results indicated that the reaction product contained the major product [[II]] 2b and a minor amount of [[III]] 3b. The major product [[II]] 2b (1S,2S,4R)-2-N-morpholinyl-1-methyl-4-(1-methylethenyl)-cyclohexanol was further purified by re-crystallization in isopropanol. ¹H NMR δ_H (300 [[mHz]] MHz, [[CHCl₃]] CDCl₃): 1.15-1.32 (4H,m), 1.52 (3H,m), 1.73 (3H,s), 1.75 (3H,s), 2.05 (1H,s), 2.10 (1H,d), 2.51 (3H,m), 2.75 (2H,m), 3.7 (4H,m), 4.72 (1H,m), 4.9 (2H,dd). ¹³C NMR δ_C (300 [[mHz]] MHz, CHCl₃): 14.19, 20.90, 22.34, 25.12, 26.24, 35.71, 38.96, 45.37, 52.01, 60.24, 67.45, 72.68, 110.97, 145.44.--

Please amend the paragraph beginning at page 10, line 6, as follows:

-- PREPARATION OF ~~(1S,2S,4R)-2-(N-morpholinyl)-1-methyl-4-(1-methylethenyl)-cyclohexanol~~ (1S,2S,4R)-2-(N-morpholinyl)-1-methyl-4-(1-methylethenyl)-cyclohexanol--

Please amend the paragraph beginning at page 10, line 8, as follows:

-- ~~(1R)-trans-1-methyl-4-(1-methylethenyl)-2-cyclohexene-1-ol~~ (1S,2S,4R)-2-(N-morpholinyl)-1-methyl-4-(1-methylethenyl)-cyclohexanol was synthesized as in Example 1, substituting lithium bromide in place of the lithium acetate in the reaction. A similar product mixture of Formula [[I]] 2b and [[II]] 3b was seen, with the ratio of [[II]] 2b to [[III]] 3b being greater than [[1:20]] 20:1. The product was further purified and isolated by recrystallization in isopropanol.--

Please amend the paragraph beginning at page 10, line 16, as follows:

--(1S,2S,4R)-2-N-morpholinyl-1-methyl-4-(1-methylethenyl)-cyclohexanol was synthesized as in Example 1, substituting lithium chloride in place of the lithium acetate in the

Amendment B

Inventor(s) Name: Gu, et.al.

Attorney Docket No.: 1559 WO/US

reaction. A similar product mixture of Formula [[I]] 2b and [[II]] 3b was seen, with the ratio of [[II]] 2b to [[III]] 3b being greater than [[1:20]] 20:1. The product was further purified and isolated by recrystallization in isopropanol.--

Please amend the paragraph beginning at page 11, line 3, as follows:

--(1S,2S,4R)-2-N-morpholinyl)-1-methyl-4-(1methylethenyl)-cyclohexanol was synthesized as in Example 1, substituting aluminum oxide in place of the lithium acetate in the reaction. A similar product mixture of Formula [[I]] 2b and [[II]] 3b was seen, with the ratio of [[II]] 2b to [[III]] 3b being greater than 20:1. The product was further purified and isolated by recrystallization in isopropanol.--

Please amend the paragraph beginning at page 11, line 10, as follows:

-- PREPARATION OF ~~(1S,2S,4R)-1-METHYL-4-(1-METHYLETHENYL)-2-(N-METHYLBENZYL)-CYCLOHEXANOL~~ (1S,2S,4R)-1-METHYL-4-(1-METHYLETHENYL)-2-(N-METHYLBENZYLAMINE)-CYCLOHEXANOL:--

Please amend the paragraph beginning at page 11, line 12, as follows:

--10.00 g of (+)-limonene oxide was dissolved into 90 ml of ethanol and placed into a 250 ml 3 neck round bottom flask. 7 g of LiOAc hydrate was added to the above mixture and stirred at 50° C for about 30 minutes. 20 g of benzylmethylamine was dissolved into 30 ml of EtOH and was added drop-wise into the reaction mixture over 10 minutes. The reaction mixture was continuously stirred at 50° C for about 16 hours. The solvent was distilled off under vacuum to give light yellow oil. The oil was dissolved into 200 ml of CHCl₃ and the solution was washed with 100 ml of water twice, 100 ml of brine one and dried with anhydrous MgSO₄. The solid was removed by filtration and solvent was removed to give light yellow oil. HPLC

Amendment B

Inventor(s) Name: Gu, et.al.

Attorney Docket No.: 1559 WO/US

analysis showed the major product is [[the II] 2b with some [[III] 3b. The ~~(1S,2S,4R)-1-methyl-4-(1-methylethenyl)-2-(N-methylbenzyl)-cyclohexanol~~ (1S,2S,4R)-1-methyl-4-(1-methylethenyl)-2-(N-methylbenzylamine)-cyclohexanol was purified by recrystallization of its HCL salt in isopropanol. ¹H NMR δ_H (300 [[mHz]] MHz, [[CHCl₃]] CDCl₃): 1.53 (4H,m), 1.81 (3H,s), 1.92 (2H,m), 2.35 (1H,d), 2.90 (3H,s), 3.35 (3H,s), 3.70 (1H,d), 4.5 (2H,dd), 4.93 (2H,d), 7.3-7.7(5H,m). ¹³C NMR [[δ_H]] δ_C (300 [[mHz]] MHz, CHCl₃): 22.7, 24.5, 28.65, 39.3, 39.5, 49.8, 50.4, 73.9, 112.1, 128.3, 128.41, 129.8, 133.1, 133.4, 144.2, 165.0.--

Please amend the paragraph beginning at page 12, line 9, as follows:

--(1S,2S,4R)-2-(N-piperidiny)-1-methyl-4-(1-methylethenyl)-cyclohexanol was synthesized as described in example 5, by utilizing piperidine as the amine. A similar product mixture of Formula [[I] 2b and [[II] 3b was seen, with the ratio of [[II] 2b to [[III] 3b being greater than [[1:20]] 20:1. The product, (1S,2S,4R)-2-N-piperidiny)-1-methyl-4-(1methylethenyl)-cyclohexanol was further purified and isolated by recrystallization in isopropanol.--

Please amend the paragraph beginning at page 12, line 18, as follows:

--(1S,2S,4R)-2-(N-pyrrolidiny)-1-methyl-4-(1-methylethenyl)-cyclohexanol was synthesized as described in example 5, by utilizing pyrrolidine as the amine. A similar product mixture of Formula [[I] 2b and [[II] 3b was seen, with the ratio of [[II] 2b to [[III] 3b being greater than [[1:20]] 20:1. The product, (1S,2S,4R)-2-N-pyrrolidiny)-1-methyl-4-(1methylethenyl)-cyclohexanol was further purified and isolated by recrystallization in isopropanol.--

Please amend the paragraph beginning at page 13, line 2, as follows:

Amendment B

Inventor(s) Name: Gu, et.al.

Attorney Docket No.: 1559 WO/US

-- PREPARATION OF ~~(1S,2S,4R)-2-(N-DIISOPROPYL)-1-METHYL-4-(1-METHYLETHENYL)-CYCLOHEXANOL~~ (1S,2S,4R)-2-(N-DIISOPROPYLAMINE)-1-METHYL-4-(1-METHYLETHENYL)-CYCLOHEXANOL--

Please amend the paragraph beginning at page 13, line 4, as follows:

--~~(1S,2S,4R)-2-(N-diisopropyl)-1-methyl-4-(1-methylethenyl)-cyclohexanol~~ (1S,2S,4R)-2-(N-diisopropylamine)-1-methyl-4-(1-methylethenyl)-cyclohexanol was synthesized as described in example 5, by utilizing diisopropylamine as the amine. A similar product mixture of Formula [[I]] 2b and [[II]] 3b was seen, with the ratio of [[II]] 2b to [[III]] 3b being greater than 20:1. The product, ~~(1S,2S,4R)-2-(N-diisopropyl)-1-methyl-4-(1-methylethenyl)-cyclohexanol~~ (1S,2S,4R)-2-(N-diisopropylamine)-1-methyl-4-(1-methylethenyl)-cyclohexanol was further purified and isolated by recrystallization in isopropanol.--

Please amend the paragraph beginning at page 13, line 13, as follows:

-- Dissolve 15 g of a Formula [[II]] 2b from example 1 or 2 into 30 ml of EtOH, added 50% H₂O₂ into slowly over 30 minutes. The reaction mixture was stirred at 50° C for about 4 hours, and the reaction progress was monitored by HPLC. Upon the complete conversion of [[the II]] 2b to [[IV]] 4b as indicated by HPLC, catalytic amount of 5% Pd/C was added to the reaction mixture to decompose the unreacted hydrogen peroxide and the reaction mixture was continue stirred for about one hour. The reaction mixture was tested negative with the peroxides test strip. The catalyst was removed via filtration and solvent was evaporated under vacuum, a white solid was obtained. ¹H NMR δ_H (300 [[mHz]] MHz, [[CHCl₃]] CDCl₃): 1.15-1.32 (4H,m), 1.52 (3H,m), 1.73 (3H,s), 1.75 (3H,s), 2.05 (1H,s), 2.10 (1H,d), 2.51 (3H,m), 2.75 (2H,m), 3.7

Amendment B

Inventor(s) Name: Gu, et.al.

Attorney Docket No.: 1559 WO/US

(4H,m), 4.72 (1H,m), 4.9 (2H,dd).). ^{13}C NMR $[[\delta_{\text{H}}]] \delta_{\text{C}}$ (300 $[[\text{mHz}]]$ MHz, CHCl_3): 14.19, 20.90, 22.34, 25.12, 26.24, 35.71, 38.96, 45.37, 52.01, 60.24, 67.45, 72.68, 110.97, 145.44.--

Please amend the paragraph beginning at page 14, line 8, as follows:

--21 g (0.08 mol) of Formula $[[\text{(VI)}]]$ 6b and 265 ml of toluene were charged in a reactor equipped with a Dean's trap and condenser. Silica oxide, 5 g, was added to the reaction mixture. The reaction mixture was heated to reflux for about 6 hours and followed by HPLC. Upon completion of the reaction the reaction mixture was filtered and the solvent evaporated under vacuum to give a dark colored oily residue. The product, (1R)-trans-1-methyl-4-(1-methylethenyl)-2-cyclohexene-1-ol, was recovered as a light yellow oil by fractional distillation under vacuum at 85°C. $[\alpha]_{\text{D}}=63.9^\circ \text{C}$ (c=0.325 CHCl_3). ^1H NMR δ_{H} (300 $[[\text{mHz}]]$ MHz, $[[\text{CHCl}_3]]$ CDCl_3): 1.28 (3H,s), 1.40-1.66 (4H,m), 1.73 (3H,s), 1.80-1.86 (1H,m), 2.67 (1H,m), 4.73 (1H,s), 4.78 (1H,s) 5.67 (1H,d,J=11 Hz), 5.68 (1H,d,J=11 Hz). ^{13}C NMR $[[\delta_{\text{H}}]] \delta_{\text{C}}$ (300 $[[\text{mHz}]]$ MHz, CHCl_3): 20.81, 24.82, 29.35, 36.63, 43.42, 67.47, 110.55, 132.23, 133.92, 148.22.--